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ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 05/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/038,835	BAI ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2004*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *18-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status

1. Claims 1-27 are pending.

Claims 1-17 and 27 are rejected.

Claims 18-26 are withdrawn from consideration as Applicant correctly notes.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-3, 6, 9-11 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register:

December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification. In this case, all of the claims comprises primers, which according to claim 9 may be up to 1000 nucleotides in length, which are not described in the specification. The genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named SEQ ID Nos. Thus, applicant has express possession of only the disclosed SEQ ID NO:s 1-54, in a genus which comprises hundreds of billions of different possibilities. Here, no common element or attributes of the sequences are required for the primers. That is, for example, the only requirement of the adenovirus primer is that the primer be derived from the hexon gene of adenovirus. There are over 50 known strains of adenoviruses and the specification has provided sequence information regarding only one. The specification has not identified other primers which will detect the known strains of adenovirus, much less the many unknown strains which are continually being discovered. For example, in the post filing date art, Yoshifumi et al (J. Med. Virol. (2003) 69:215-19) teaches the identification of three new genome types of Adenovirus 7 in February of 2003. These types were not described by the specification, were not available in the prior art, and yet the claims encompass primers derived from these types, unknown to the specification. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided. Further, these

claims encompass allelic variants including insertions and mutations and only specific nucleic acid sequences have been provided. No written description of alleles has been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the primers as derived from, for example, the hexon gene of adenovirus, lacks any specific structure. This is precisely the situation of naming a type of material which is generally known to likely exist, but, except for the specific disclosed primers, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to any primer derived from adenovirus hexon region.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a primer, without any definition of the particular primers claimed.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which comprise primers in the various respiratory viruses. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Response to Arguments – 112, Written Description

4. Applicant's arguments filed April 15, 2004 have been fully considered but they are not persuasive.

Applicant argues that there is sufficient description of species in the claimed genus to overcome the written description rejection and Applicant relies upon Example 9 of the written description guidelines to support this position. Applicant is incorrectly applying the fact pattern of Example 9 to the current facts for a number of reasons.

First, and most simply, the claim in example 9 incorporates two elements absent from the current claim. The claim incorporates a specific sequence with a specific SEQ ID NO. Also the claim incorporates specific hybridization conditions. Both of these elements are lacking from Applicant's claims and so the facts are therefore significantly different. Applicant lacks any structure whatsoever, while the example requires a specific structure. So consonant with the case law in Lilly, Enzo and the other written description decision of the Federal Circuit, it is clear that the current claims fail to meet the written description requirement because there is literally no structure whatsoever. Further, the absence of specific hybridization conditions also differentiates the claims because these conditions, as related to the particular claimed SEQ ID NO: are responsible for the conclusion that there would be insubstantial variation. No such conditions and no SEQ ID Nos are in the currently rejected claims.

Second, when Applicant relies upon the analysis of the written description guidelines, this analysis is based upon the assumption that there will be insubstantial variation, as noted in many of the examples including example 9. However, Applicant's analysis is flawed since there is no expectation in the instant case of insubstantial variation because the functional limitation devolves solely to the ability of the nucleic acid to hybridize. This is not like example 9, where the functional limitation involved a protein which retained adenylate cyclase activity. In the example 9 case, the argument of insubstantial variation was that there was an expectation that stringently hybridizing proteins which retained the specific function of stimulating adenylate cyclase would differ insubstantially.

In the current case, there is no such expectation of insubstantial variation. There is NO functional requirement that is tied to structure whatsoever, similar to the adenylate cyclase activity. Hybridization is an inherent capability of nucleic acids, and amplification, in particular, can be achieved with non specific primers. Many methods, ranging from ARMS to differential display, specifically rely on the fact that nonspecific unrelated nucleic acids are capable of amplifying specific targets. So the argument by Applicant that there would be insubstantial variation is not correct since the function of hybridizing and amplifying does not limit the nucleic acid in any significant way.

Therefore, since the claims differ very substantially from those in Example 9 of the written description guidelines and fail to comply with the guidance given by the Federal Circuit, the rejection under written description is maintained.

Claim Rejections - 35 USC § 112 – second paragraph

5. Claims 1-17 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In the sequence listing of elected SEQ ID Nos: 20, 35, 38, 39, 49 and 50, there are ambiguity codes such as K meaning G or T/U as well as other codes. However, the claims are indefinite as to whether they are intended to encompass a mixture of primers for the primers with ambiguity codes or a single primer with one of the two sequences. That is, for example, in SEQ ID NO: 20, it is unclear if the actual primer product is ctgggataacatc**G**tcaaactc or ctgggataacatc**T**tcaaactc or ctgggataacatc**U**tcaaactc or some combination of these primers. Any clarifying amendment should clearly identify basis

for the position taken in the specification to avoid new matter issues. For purposes of the prior art rejections, it will be assumed that the primer product is one or the other of the nucleotides, but not a mixture, since page 7 of the specification states "Furthermore, at positions where single nucleotide polymorphisms occur, nucleotide variations are allowed in primers and probes described in this invention. As single nucleotide polymorphisms may be associated with a particular genotype or phenotype, these primers and probes can be used to distinguish and categorize different virus strains." This quote indicates that the primers are not mixtures but are, in fact, strain specific primers. Consequently, the primers are a particular sequence.

Response to Arguments – 112, second paragraph

6. Applicant's arguments filed April 15, 2004 have been fully considered but they are not persuasive.

Applicant's arguments fail to address the actual issue. The issue is not a sequence rules issue and no objection was made that the claims fail to comply with the Sequence Rules. The issue is a true interpretational question, which is what does a primer with an ambiguous nucleotide consist of? Applicant's response that the sequences are in the table in the specification does not resolve this question because these tables also use the ambiguity codes. As noted in the rejection, it is unclear what the primer mixture consists of. Using SEQ ID NO 20 again as an example, it is indefinite whether the primer used has a G at the ambiguous position, a T at that position, a U at that position, or whether there is a primer mixture which has all three possibilities at that position. Until this is resolved, the claims remain indefinite.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by Zuckerman et al (J. Virol. Methods (1993) 44:35-44).

Zuckerman et al teaches a set of nucleic acids comprising:

Zuckerman teaches detection of influenza B using primers to the hemagglutinin-neuraminidase gene (see page 37 and page 39) including

A nucleic acid containing an oligonucleotide selected from the hemagglutinin-neuraminidase gene region of influenza virus B (see page 39, specifically, primer A, for example, TTTCTAATATCCACAAAATGA, which is 21 nucleotides in length).

The claim uses the alternative "or" language, indicating that only one of the two nucleic acids is required.

Response to Arguments – 102 rejection

9. Applicant's arguments filed April 15, 2004 have been fully considered but they are not persuasive.

Applicant argues, with regard to Zuckerman in the previous 103 rejection, that the hemagglutinin protein is not the same as hemagglutinin-neuraminidase. The proteins are identical in name and the sequence is identical. Therefore, in the absence

of evidence that these proteins differ, the rejection will be maintained. MPEP 716.01(c) makes clear that

> "The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant."

Here, the statements regarding any such differences must be demonstrated, not simply argued.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1-3, 6, 9-11 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grondahl et al (J. Clin. Microbiol. (1999) 37(1):1-7) in view of Echevarria et al (J. Clin. Microbiol. (1998) 36(5):1388-1391) and further in view of Osiowy et al (J. Clin. Microbiol. (1998) 36:3149-3154) and further in view of Zuckerman et al (J. Virol. Methods (1993) 44:35-44).

Grondahl teaches a set of nucleic acids designed to detect 9 different respiratory virus samples (see abstract) comprising:

A second pair of primers containing oligonucleotides selected from the hexon region of Adenovirus which are between 14-40 nucleotides in length (see page 2, column 1),

A third pair of primers containing oligonucleotides selected from human parainfluenza virus 1 which are between 14-40 nucleotides in length (see page 2, column 1),

A fourth pair of primers containing oligonucleotides selected from human parainfluenza virus 3 which are between 14-40 nucleotides in length (see page 2, column 1),

A fifth pair of primers containing oligonucleotides selected from human respiratory syncytial virus which are between 14-40 nucleotides in length (see page 2, column 1),

A sixth pair of primers containing oligonucleotides selected from the nonstructural protein gene region of human influenza A virus which are between 14-40 nucleotides in length (see page 2, column 1),

A seventh pair of primers containing oligonucleotides selected from human influenza B virus which are between 14-40 nucleotides in length (see page 2, column 1).

Grondahl does not teach detection of human parainfluenza virus 2, nor primers to the hemagglutinin-neuraminidase of the human parainfluenza virus.

Echevarria teaches detection of human parainfluenza virus 2 in a multiplex assay (see abstract) and teaches primers drawn to the hemagglutinin-neuraminidase of the virus (see page 1388, subheading "primer design and preparation").

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to detect human parainfluenza virus 2 in the multiplex assay of Grondahl, which assay was designed to detect organisms causing respiratory tract infections since Echevarria recognizes a problem in assays which rely on detection of only human parainfluenza viruses 1 and 3, stating "RT-PCR assays for the detection of HPIVs have been described, but they have been limited to the detection of HPIV3 or HPIV1 and HPIV3, without distinguishing between the two serotypes (see page 1389, column 2)." Echevarria solves this problem of a failure to detect the medically important human parainfluenza virus 2, stating "In contrast, our multiplex assays both detect and differentiate all three medically important HPIV serotypes and provide a sensitive and specific means of identifying HPIVs directly from clinical specimens (see page 1389,

column 2)." Echevarria further motivates the combination of this assay with other multiplex assays, noting "Since primers for other respiratory virus can be added to the reaction mixture, the efficiencies of these assays can potentially be further improved (see page 1390, column 1, last sentence to column 2)." So an ordinary practitioner would have been motivated to include Echevarria's human parainfluenza virus 2 primers in the multiplex primer set of Grondahl in order to detect all three medically important HIPV serotypes as well as improve the efficiency, sensitivity and specificity of the assay to permit identification of each of the possible causative viral agents.

Grondahl in view of Echevarria do not teach selection of primers from the nucleocapsid (also called nonstructural protein 2) gene of RSV or from the hemagglutinin-neuraminidase influenza B virus.

Osiowy also teaches a multiplex assay for detection of respiratory viruses and teaches selection of the N gene of RSV (see table 1, page 3150).

Zuckerman teaches detection of influenza B using primers to the hemagglutinin-neuraminidase gene (see page 37 and page 39).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to detect the human respiratory viruses desired for detection by Grondahl in view of Echevarria using primers directed towards other genes which provided specific results for two reasons. First, Osiowy (see page 3153, column 2, last two sentences) and Zuckerman (see pages 39, 42) both teach that the primers drawn to the specific genes used are specific, and highly sensitive, thus providing a direct

motivation to use these primers. Second, the genes fundamentally represent functional equivalents, since the prior art cited above of Grondahl, Osiowy and Zuckerman recognizes that each of these genes can be used for detection of the virus of interest. MPEP 2144.06 notes " Substituting equivalents known for the same purpose. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout , 675 F.2d 297, 213 USPQ 532 (CCPA 1982)."

13. Claims 4, 5, 7, 8, 12-17 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grondahl et al (J. Clin. Microbiol. (1999) 37(1):1-7) in view of Echevarria et al (J. Clin. Microbiol. (1998) 36(5):1388-1391) and further in view of Osiowy et al (J. Clin. Microbiol. (1998) 36:3149-3154) and further in view of Zuckerman et al (J. Virol. Methods (1993) 44:35-44) and and further in view of Buck et al (Biotechniques (1999) 27(3):528-536) and further in view of Genbank Accession Numbers (and one patent) which teach sequences from which the primers were derived: Human Parainfluenza Virus 1 – X55803 (04 May 1993) – SEQ ID Nos: 1, 4; Human Parainfluenza Virus 2 - X57559 (13 May 1992) – SEQ ID Nos: 5, 7; Human Parainfluenza Virus 3 – M18759 (02 August 1993) – SEQ ID Nos: 9, 11, 39; Human Adenovirus Hexon gene – M73260 (08 April 1996) – SEQ ID Nos: 24, 26; Respiratory Syncytial Virus – M11486 (29 November 2000) SEQ ID Nos: 12, 14; Influenza A –

M12594 (02 August 1993) SEQ ID Nos: 16, 18; Influenza B – U.S. Patent 5,374,717 (20 December 1994) SEQ ID Nos: 20, 22, 50.

Grondahl in view of Echevarria and further in view of Osiowy and further in view of Zuckerman teach detection of each of the claimed viruses in a multiplex PCR assay for detection of respiratory viruses. Grondahl in view of Echevarria and further in view of Osiowy and further in view of Zuckerman do not teach the sequences from which the primers and probes were derived.

The cited Genbank Accession numbers and patent teach the sequences from which the primers were derived.

The prior art is replete with discussion of primer selection, with Osiowy stating "Five sets of oligonucleotide primers were designed for RT and amplification ... according to the nucleotide sequences available from Genbank (see page 3150, column 1)." Osiowy continues "Primers for RSV were designed visually from a highly conserved area of a nucleotide sequence alignment (see page 3150, column 1)." Osiowy concludes this paragraph by stating "Primer sequences were analyzed for suitability by using PC/GENE sequence analysis software (release 6.8, Intelligenetics, Inc.) (see page 3150, column 1)."

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the primers of Grondahl in view of Echevarria and further in view of Osiowy and further in view of Zuckerman with the use of functionally equivalent primers selected from the sequences of Genbank and U.S. Patent 5,374,717 since Osiowy expressly teaches primer selection using commercially

available software and since Genbank provide such published sequences for the software program to analyze.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers and probes for the detection of respiratory viruses and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods

of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Response to Arguments – 103 rejection

14. Applicant's arguments filed April 15, 2004 have been fully considered but they are not persuasive.

Applicant argues that the N protein is not the same as NS2 as argued in the rejection and relies upon a citation to Hacking et al. This attachment was not found and so cannot be given any weight. The proteins appear to be identical for the reasons given and the sequence is the same. Therefore, in the absence of evidence that these proteins differ, the rejection will be maintained. MPEP 716.01(c) makes clear that

> "The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of

> the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant."

Here, the statements regarding any such differences must be demonstrated, not simply argued.

With regard to Applicant's arguments on the Buck reference, this is another situation where Applicant traverses without evidence. The rejection includes evidence on the equivalence of primers. Applicant argues that this differs from the claimed situation. That argument is not relevant for several reasons. First, the claims are drawn to products and no intended use in imputed to these product claims, so the primers may be used on purified nucleic acids. Second, even if the claims were used on samples, the rejection includes evidence that the primers would be expected to be equivalent in function, while Applicant provides no contrary evidence, such as an unexpected result that one of the primers functions better than an equivalent primer. In the absence of ANY evidence from Applicant, the rejection is maintained.

With regard to the issue of the size of the Genus, this can be analogized to the decision of the CAFC in *Merck & Co. v. Biocraft Laboratories, Inc.*, 874 F.2d 804, 807 (CAFC 1989). The CAFC determined in *Merck*, that the selection of a particular compound out of 1200 possible prior art compounds in the prior art genus was determined to be obvious. In *Merck*, the obviousness was based in part on the structural similiarity of the different compounds, but was substantially based upon the Court's understanding that each and every compound in the genus would have been expected to function. The court noted that "any of the 1200 disclosed combinations will produce a diuretic formulation with desirable sodium and potassium eliminating

properties." This is identical to the current case, where Applicant notes there may be about 1835 genus members, but where every member is entirely defined by the prior art, which teaches the sequence from which the members are drawn, and each would be expected to function as evidenced by Buck.

Finally, with regard to the Zuckerman reference, the same argument as above remains applicable.

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637